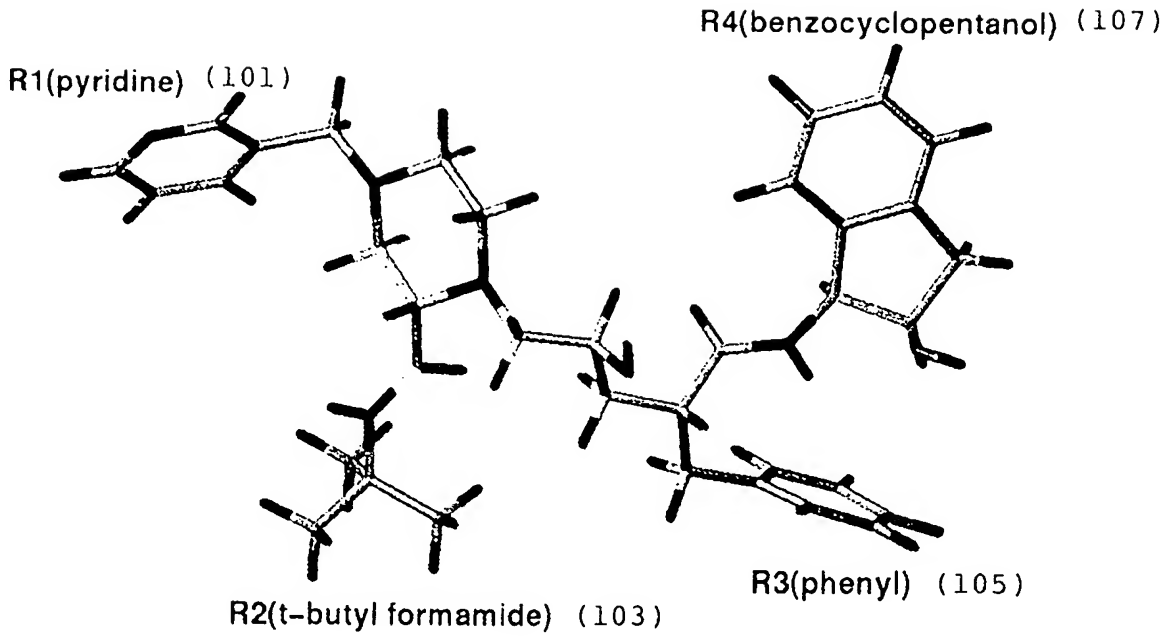

R4(benzocyclopentanol) (107)
R1(pyridine) (101)
R3(phenyl) (105)
R2(t-butyl formamide) (103)

FIG. 1

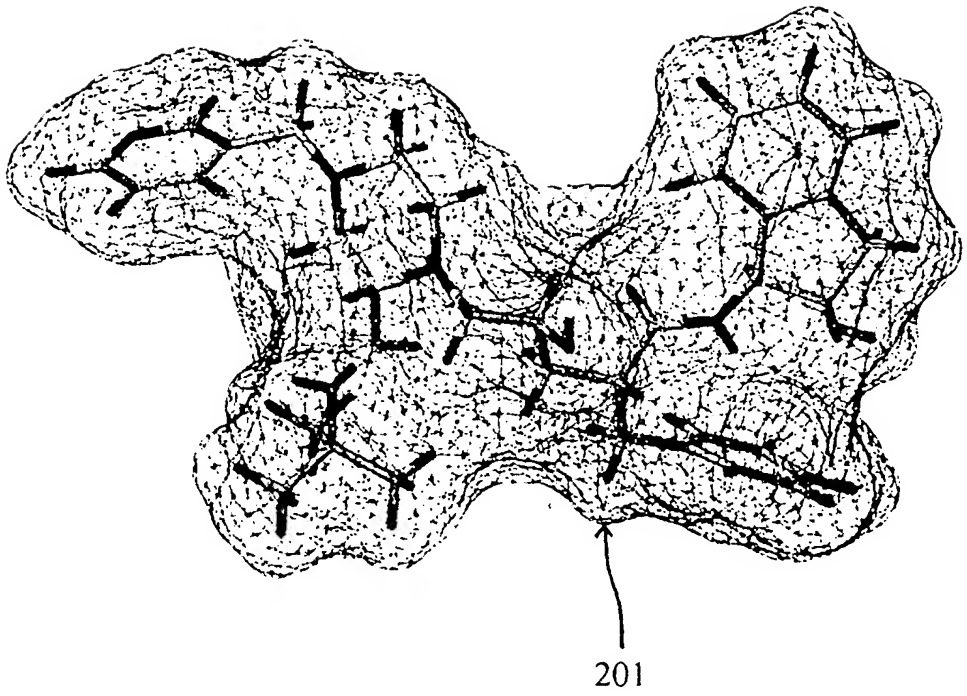



FIG. 2

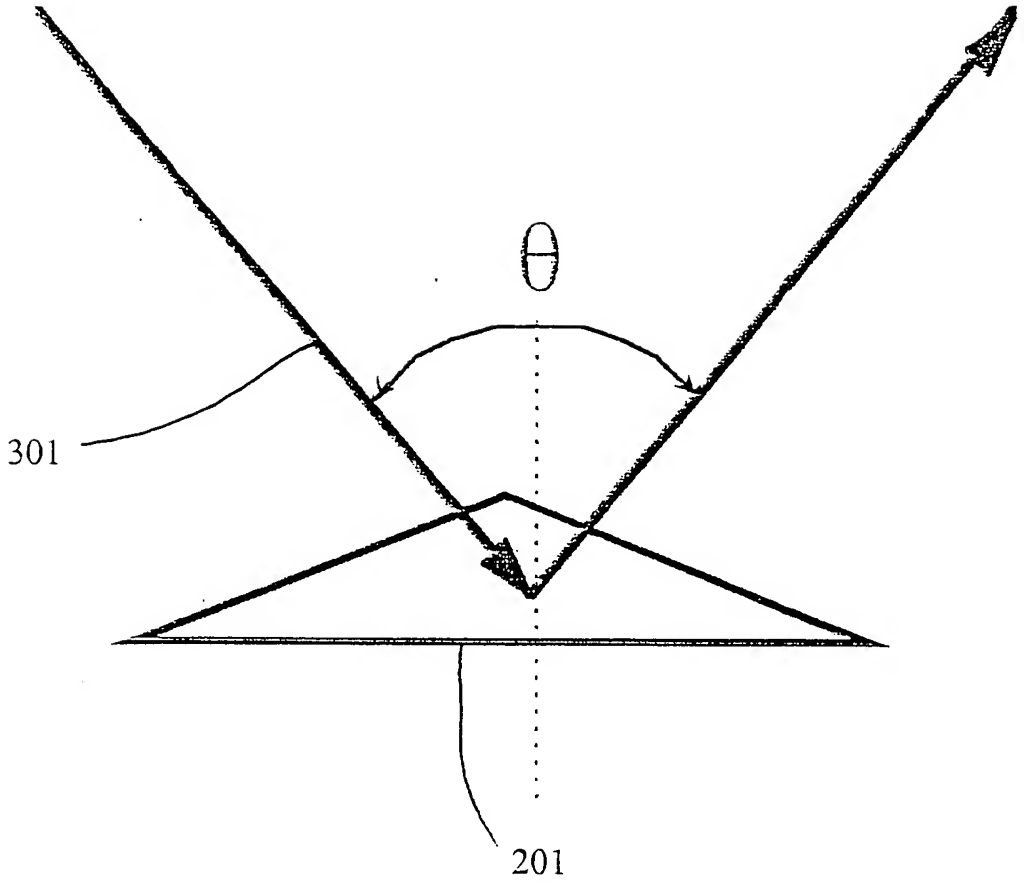



FIG. 3

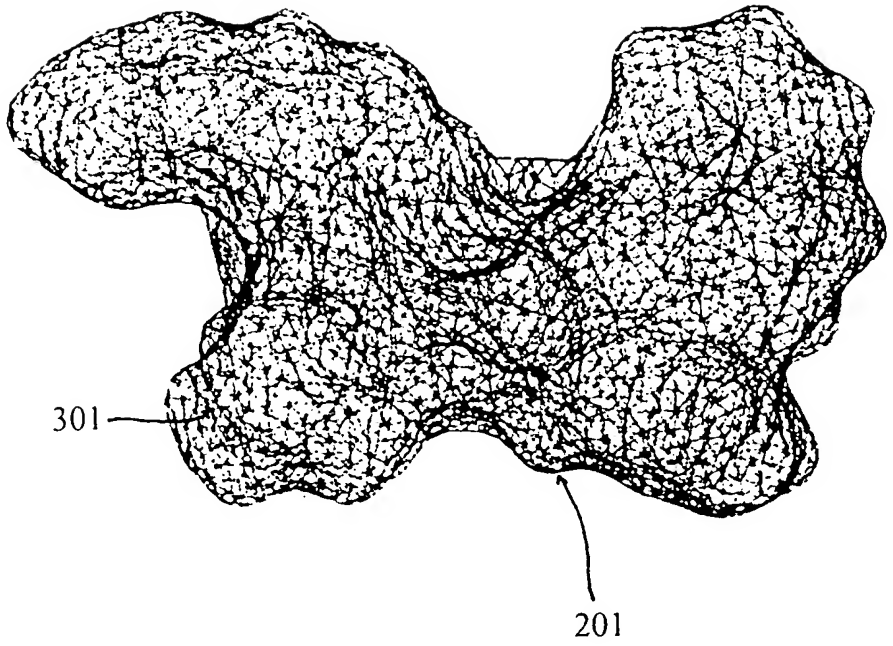



FIG. 4A

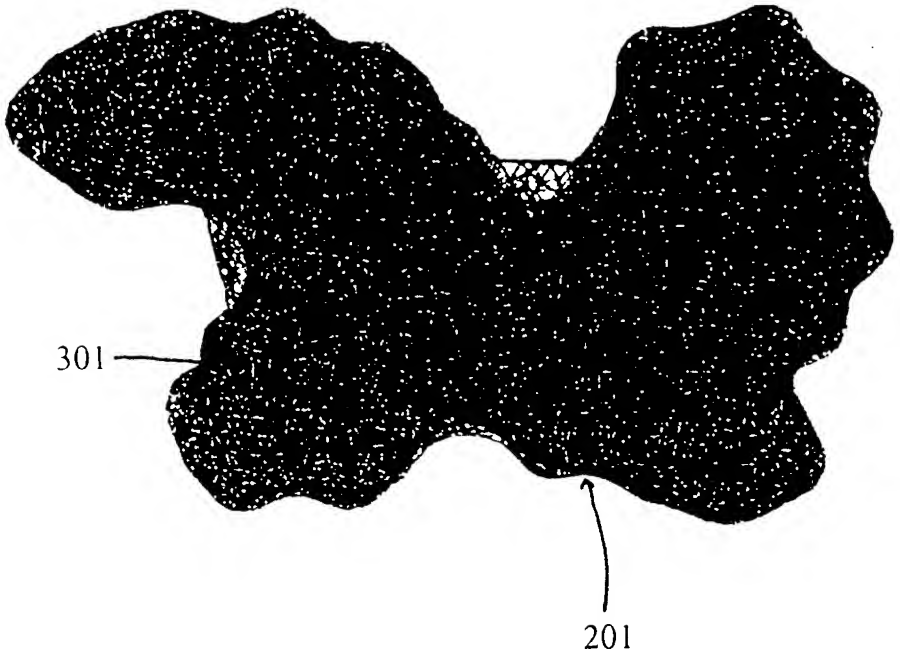



FIG. 4B

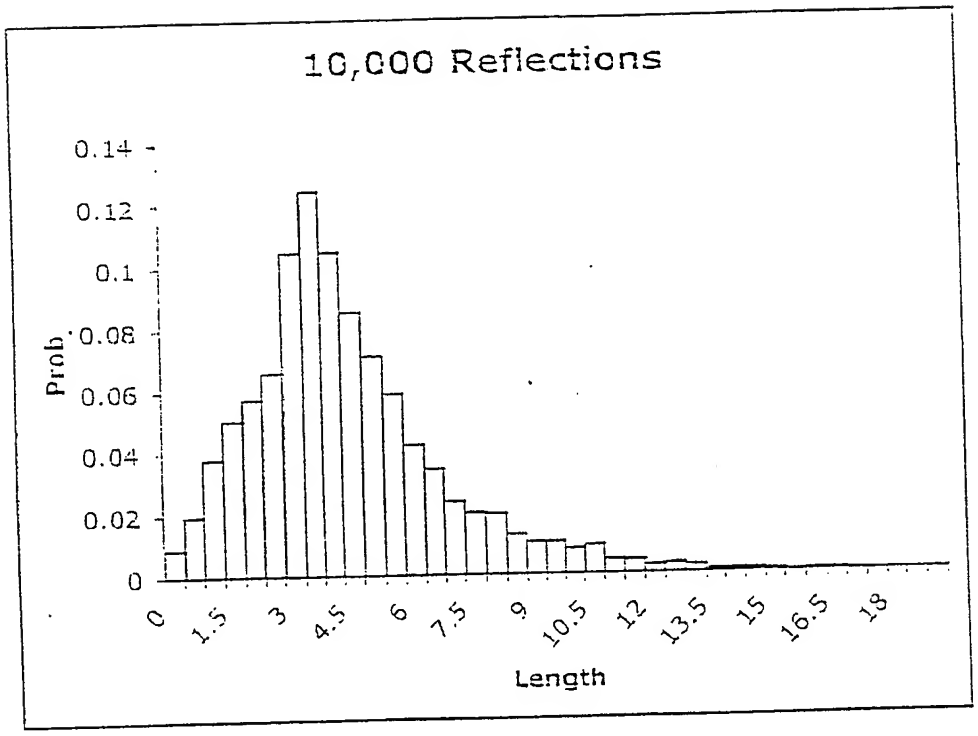

10,000 Reflections
0.14
0.12
0.1
0.08
0.06
0.04
0.02
0
Prob
0
1.5
3
4.5
6
7.5
9
10.5
12
13.5
15
16.5
18
Length

FIG. 5A

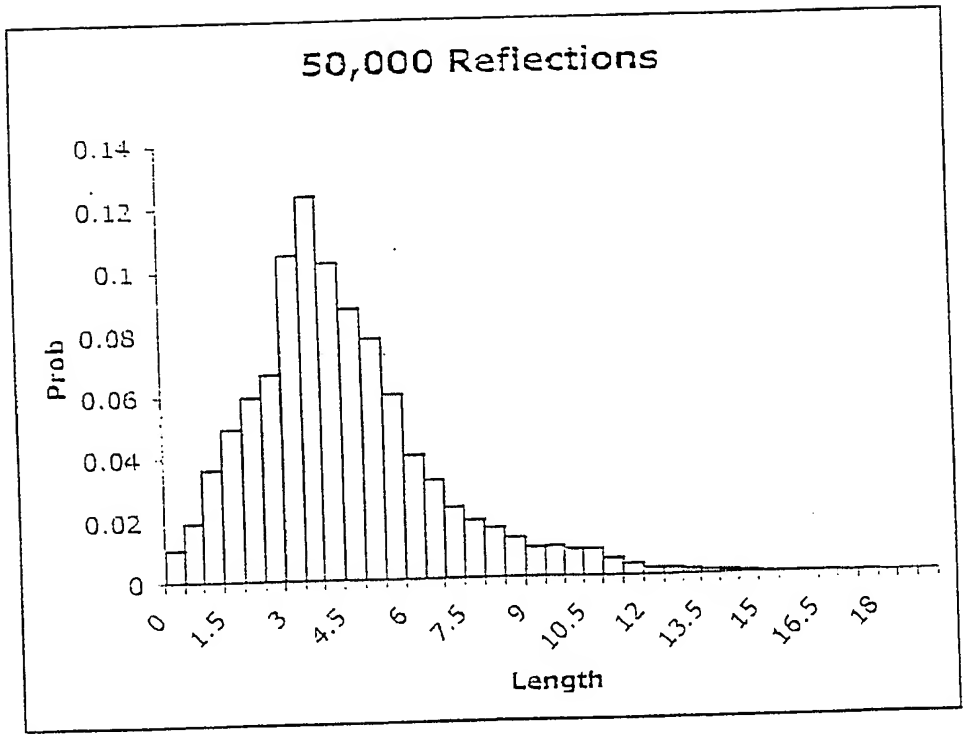

50,000 Reflections
Prob
0.14
0.12
0.1
0.08
0.06
0.04
0.02
0
0
1.5
3
4.5
6
7.5
9
10.5
12
13.5
15
16.5
18
Length

FIG. 5B

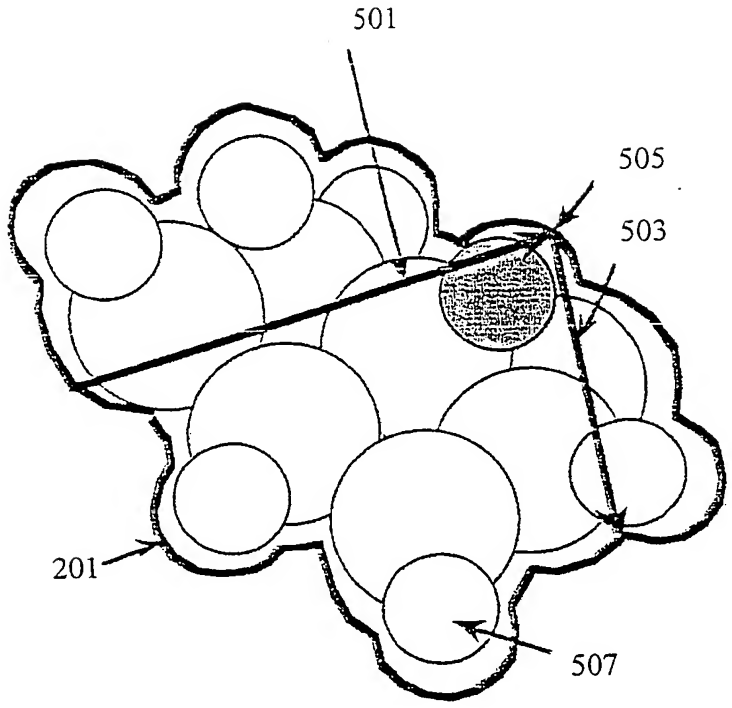



FIG. 6

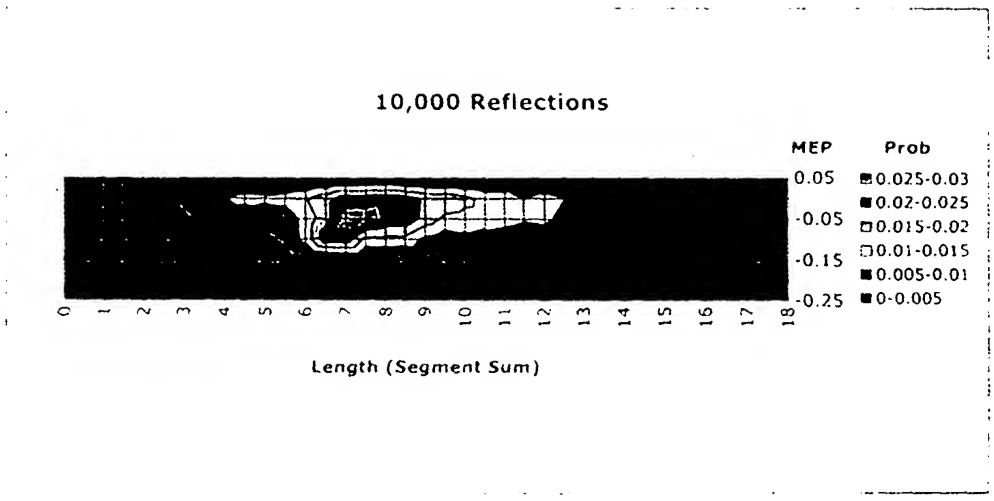

10,000 Reflections
MEP
Prob
0.05
-0.05
-0.15
-0.25
0.025-0.03
0.02-0.025
0.015-0.02
0.01-0.015
0.005-0.01
0-0.005
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18
Length (Segment Sum)

FIG. 7A

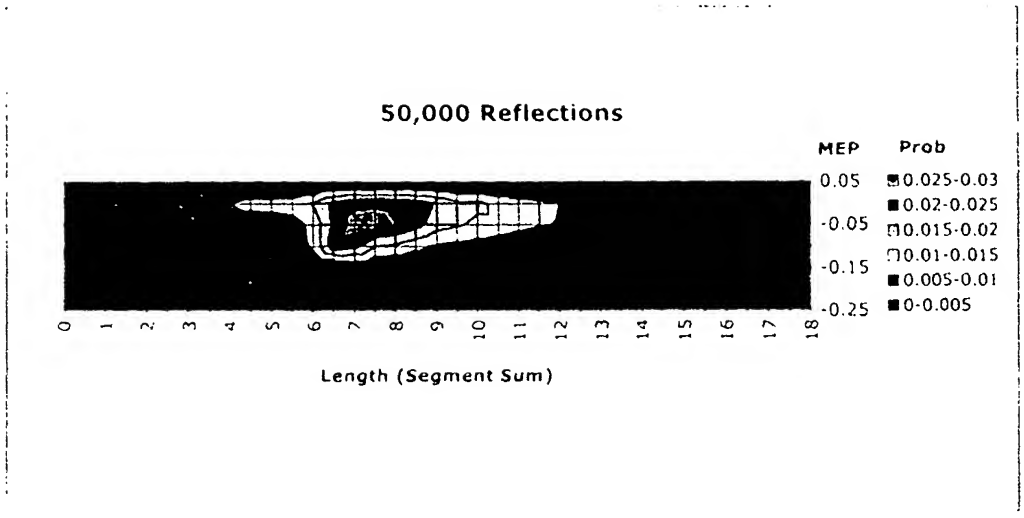

50,000 Reflections
MEP
Prob
0.05
-0.05
-0.15
-0.25
0.025-0.03
0.02-0.025
0.015-0.02
0.01-0.015
0.005-0.01
0-0.005
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18
Length (Segment Sum)

FIG. 7B

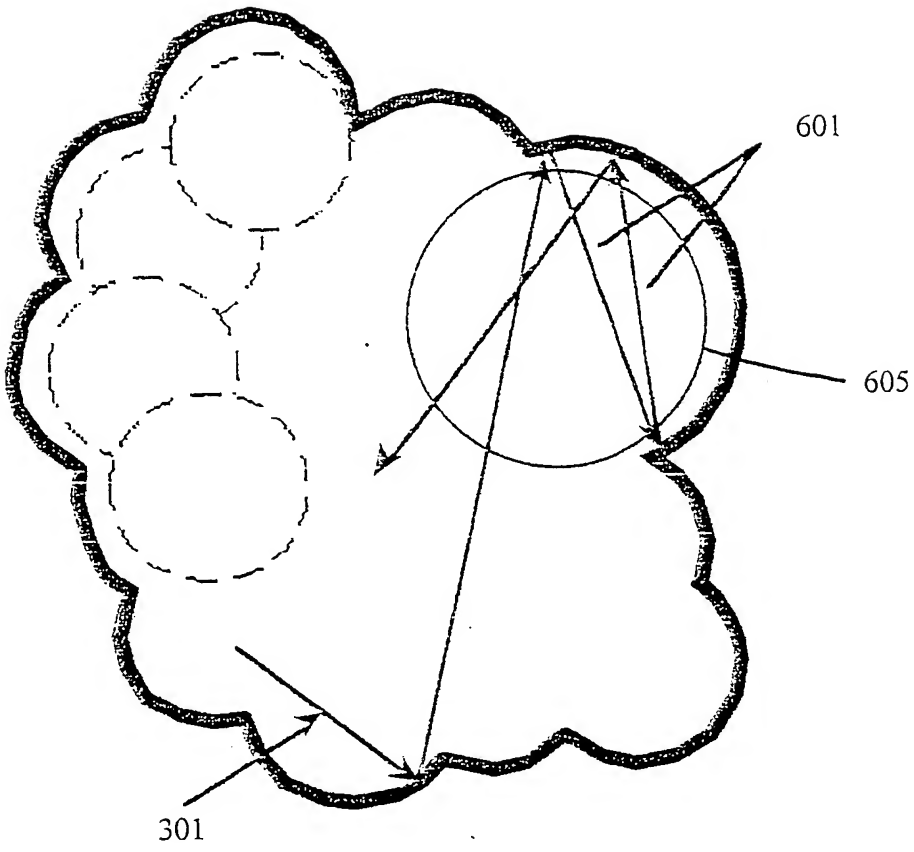



FIG. 8

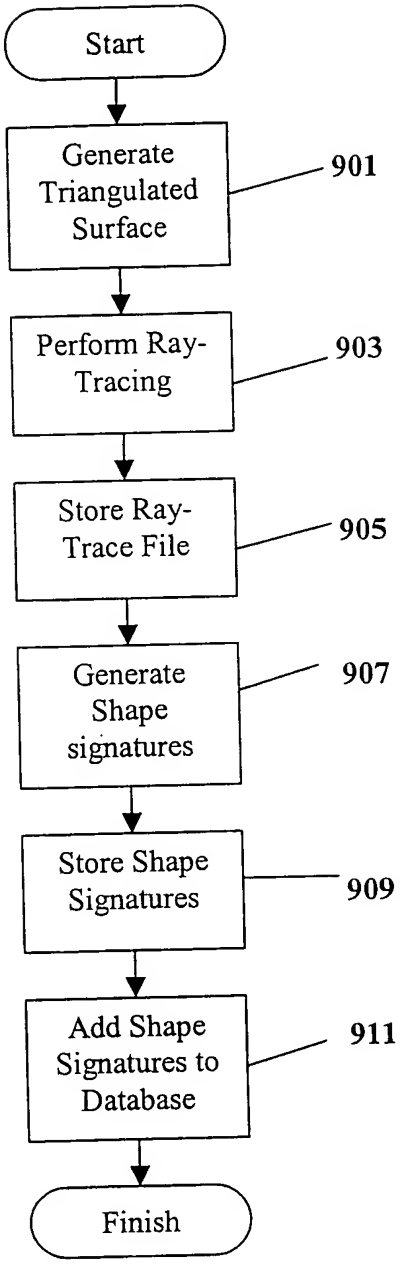

Start
Generate Triangulated Surface
901
Perform Ray-Tracing
903
Store Ray-Trace File
905
Generate Shape signatures
907
Store Shape Signatures
909
Add Shape Signatures to Database
911
Finish

FIG. 9

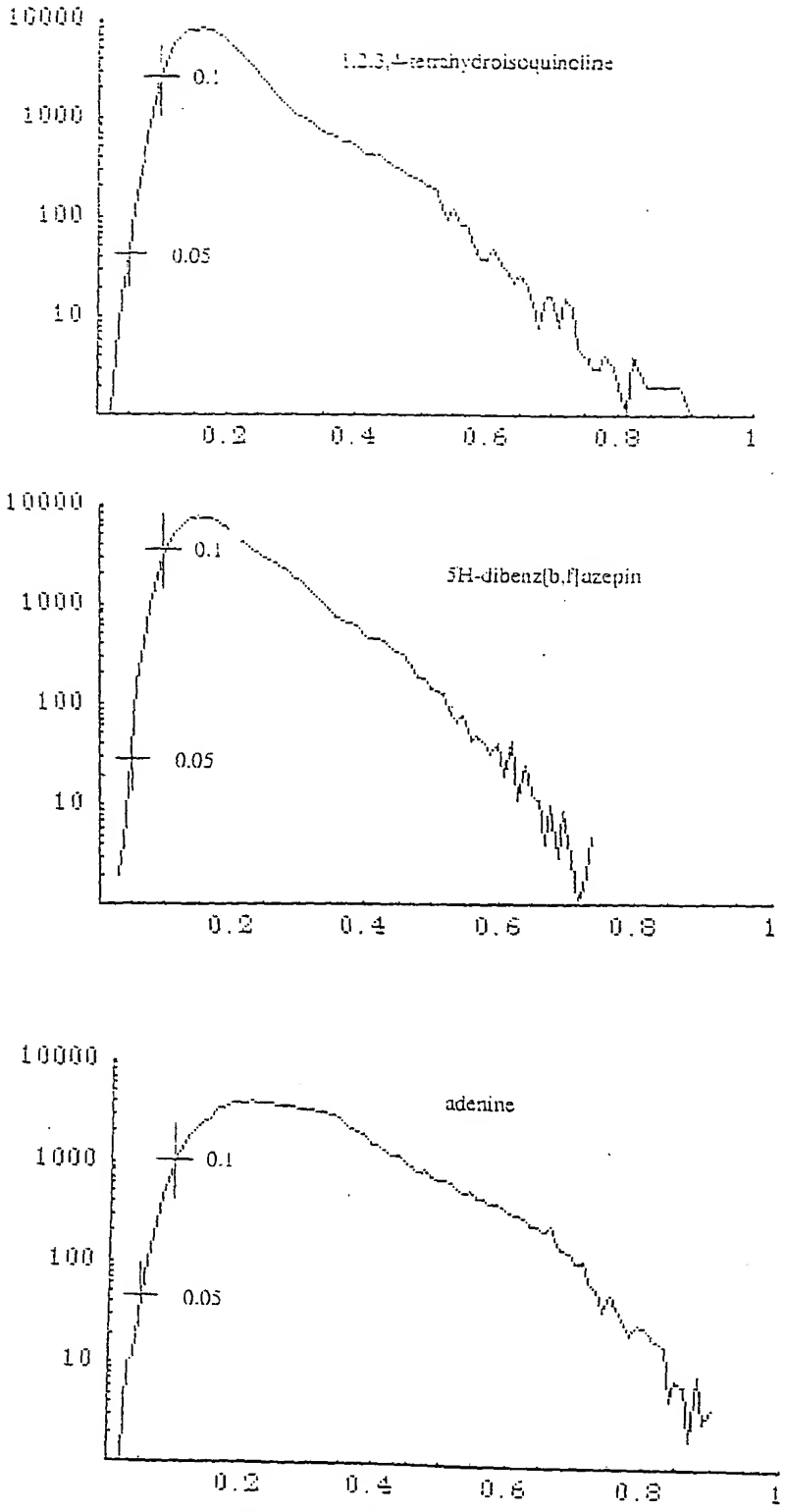

10000
1000
100
10
0.1
0.05
1,2,3,4-tetrahydroisoquinoline
0.2
0.4
0.6
0.8
1
10000
1000
100
10
0.1
0.05
5H-dibenz[b,f]azepin
0.2
0.4
0.6
0.8
1
10000
1000
100
10
0.1
0.05
adenine
0.2
0.4
0.6
0.8
1

**FIG. 10A**

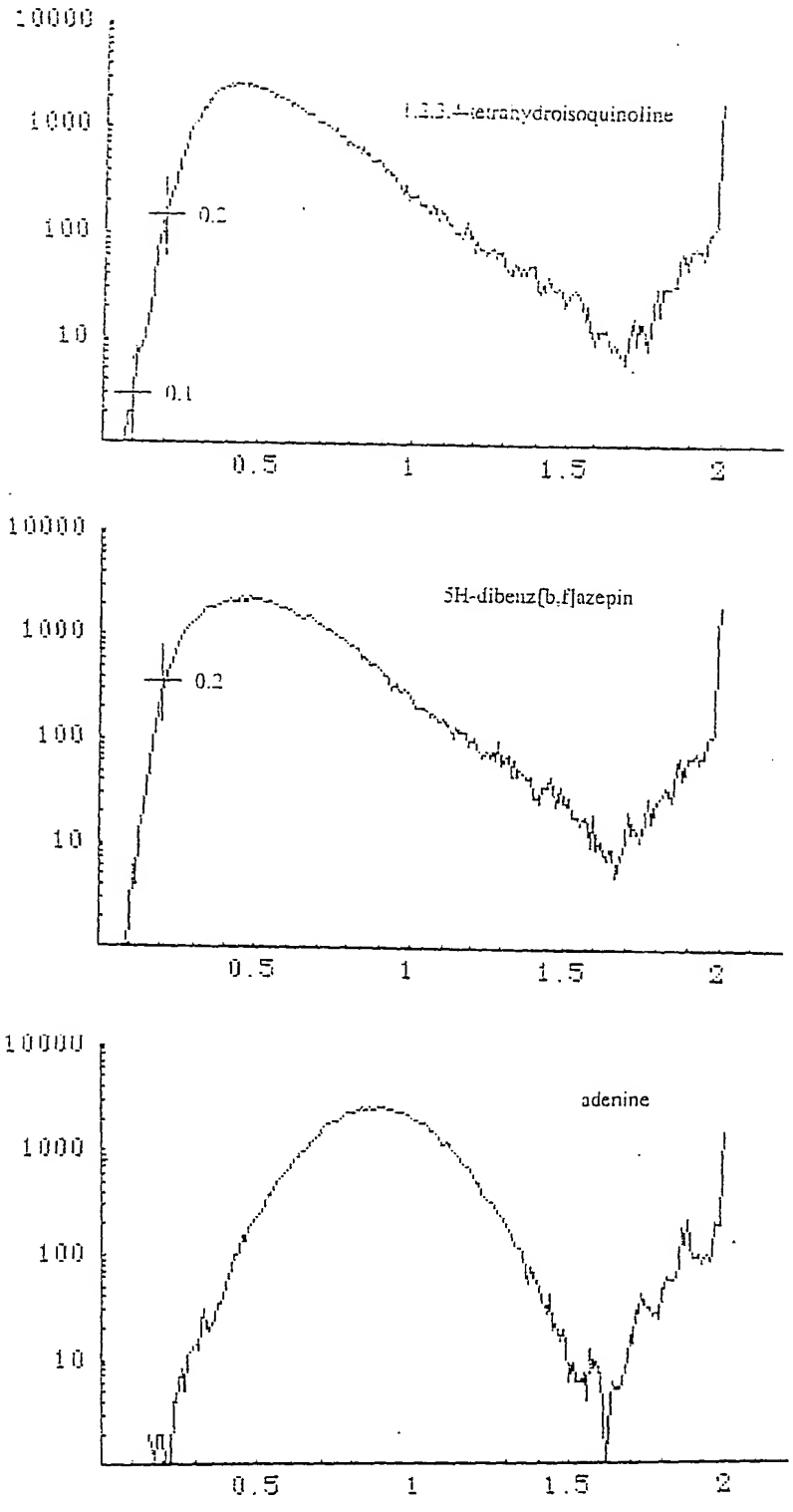

10000
1000
100
10
0.2
0.1
0.5
1
1.5
2
1,2,3,4-tetrahydroisoquinoline
10000
1000
100
10
0.2
0.5
1
1.5
2
5H-dibenz[b,f]azepin
10000
1000
100
10
0.5
1
1.5
2
adenine

FIG. 10B

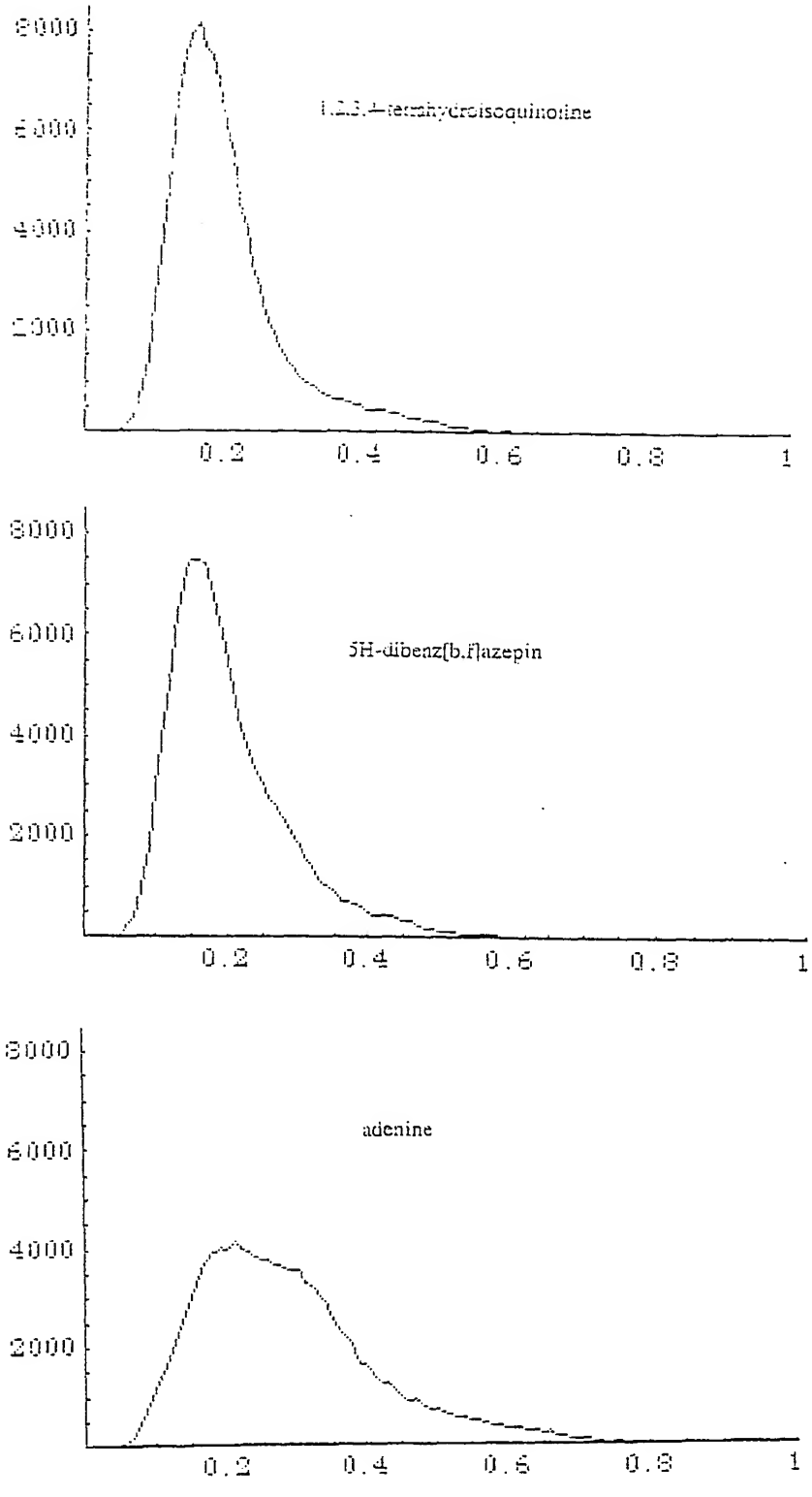

8000
6000
4000
2000
1,2,3,4-tetrahydroisoquinoline
0.2
0.4
0.6
0.8
1
8000
6000
4000
2000
5H-dibenz[b,f]azepin
0.2
0.4
0.6
0.8
1
8000
6000
4000
2000
adenine
0.2
0.4
0.6
0.8
1

FIG. 11A

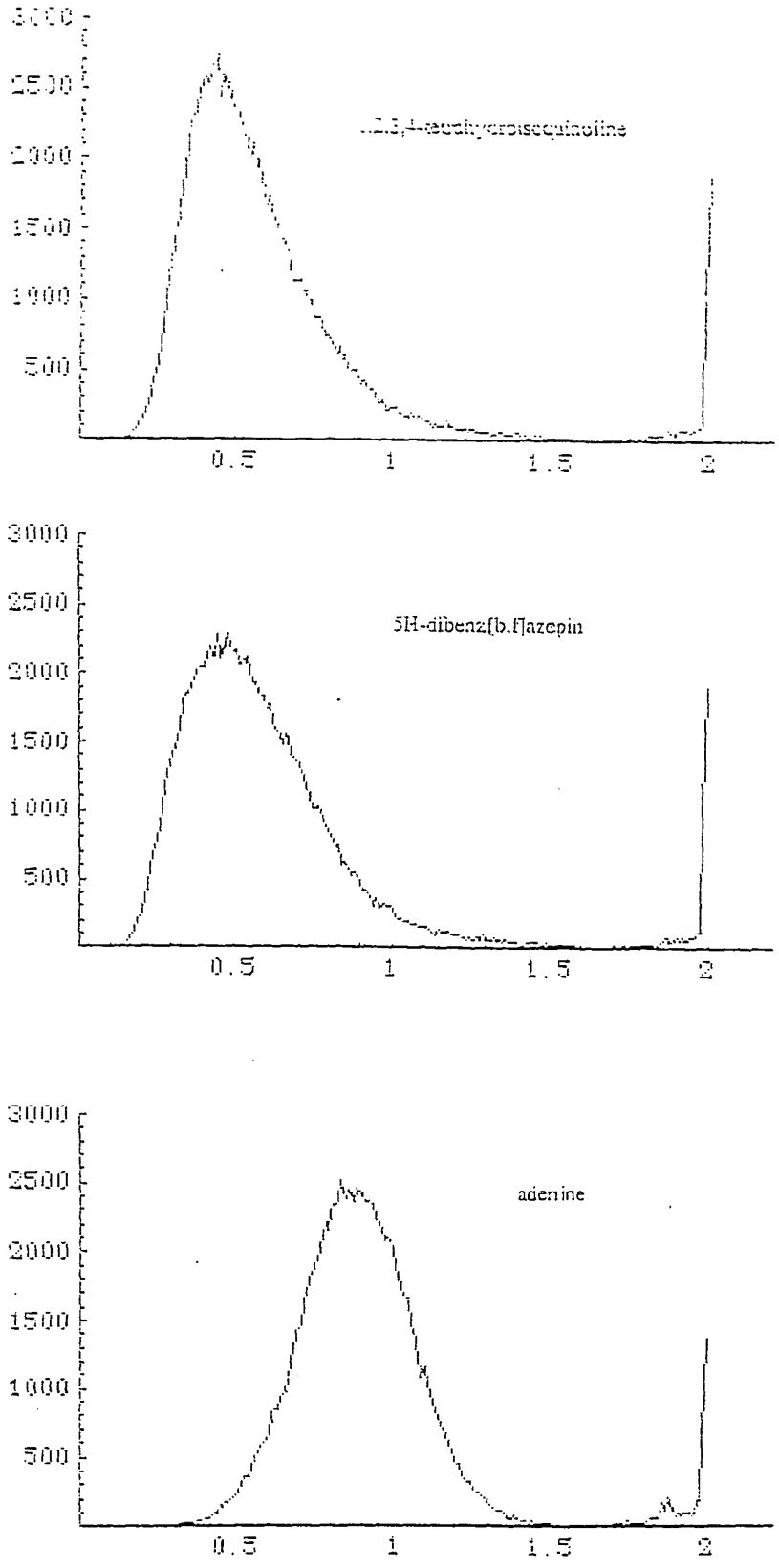

3000
2500
2000
1500
1000
500
0.5
1
1.5
2
5H-dibenz[b,f]azepin
adenine

FIG. 11B

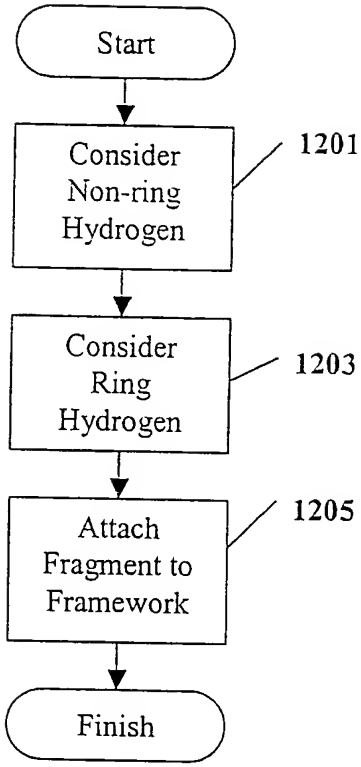

Start
Consider Non-ring Hydrogen
1201
Consider Ring Hydrogen
1203
Attach Fragment to Framework
1205
Finish

FIG. 12

FIG. 13A

FIG. 13B

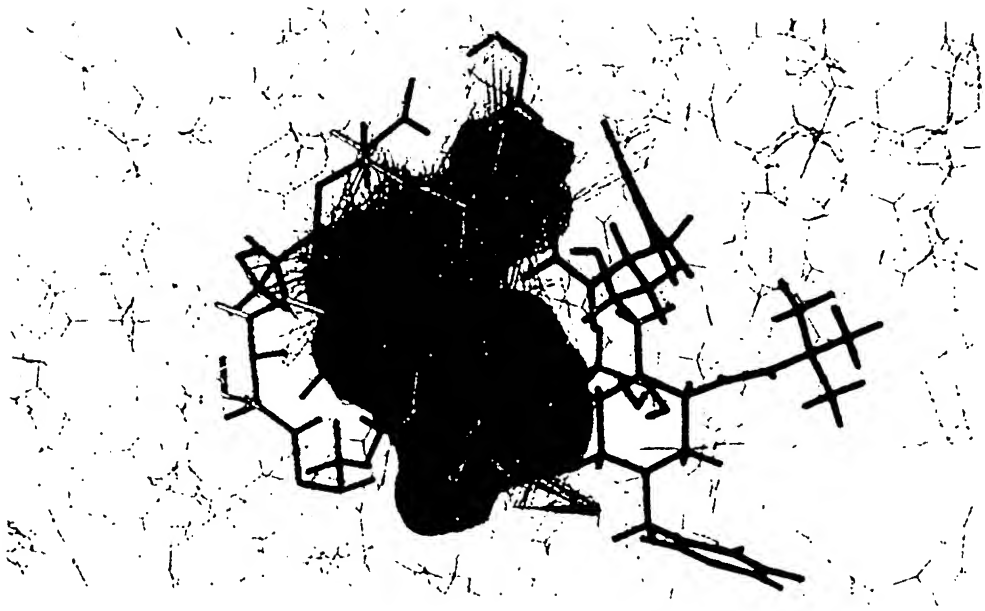


FIG. 13C

. Results for Six Query Compounds, 1-D Shape Signature Self-Comparison of Tripos Fragment using $L_1$ Metric

| QUERY | Culling | | No Culling | |
|---|---|---|---|---|
| | Hit | Score | Hit | Score |
| 1,2,3,4-tetrahydroisoquinoline | 1,2,3,4-tetrahydroquinoline | 0.0370 | 1,2,3,4-tetrahydroquinoline | 0.0173 |
| | isochroman | 0.0386 | isochroman | 0.0316 |
| | 1,2,3,4-tetrahydronaphthalene | 0.0490 | chroman | 0.0399 |
| | chroman | 0.0574 | 1,2,3,4-tetrahydronaphthalene | 0.0475 |
| | indoline | 0.0767 | indan | 0.0525 |
| 5H-dibenz[b,f]azepin | dibenzocycloheptatriene | 0.0351 | dibenzocycloheptatriene | 0.0332 |
| | dihydrophenanthrene | 0.0482 | dihydrophenanthrene | 0.0384 |
| | thioxanthene | 0.0578 | thioxanthene | 0.0466 |
| | dibenz[b,f]thiepin | 0.0695 | 5H-dibenzo[b,f]-1,4diazepine | 0.0487 |
| | 5H-dibenzo[b,f]-1,4-diazepine | 0.0800 | dibenz[b,f]thiepin | 0.0578 |
| 1,4,6-gonatriene-3,17-dione | 4,6-gonadiene-3,17-dione | 0.0502 | 4,6-gonadiene-3,17-dione | 0.0400 |
| | 1,4-gonadien-3-one | 0.0743 | 1,4-gonadien-3-one | 0.0660 |
| | 4-gonen-3-one | 0.0984 | 4-gonen-3-one | 0.0838 |
| | 1,3,5(10)-gonatriene | 0.0986 | 1,3,5(10)-gonatriene | 0.0862 |
| | 5(10)-gonen-3-one | 0.1004 | 5(10)-gonen-3-one | 0.0984 |
| α-D-glucopyranose | β -D-mannopyranose | 0.0417 | α-D-mannopyranose | 0.0376 |
| | β-D-galactopyranose | 0.0420 | β -D-mannopyranose | 0.0379 |
| | α-D-mannopyranose | 0.0559 | β-D-galactopyranose | 0.0391 |
| | α-D-galactopyranose | 0.0744 | α-D-galactopyranose | 0.0560 |
| | β-D-glucopyranose | 0.0748 | β-D-glucopyranose | 0.0766 |
| Lysine | Arginine | 0.0862 | Methionine | 0.0527 |
| | Methionine | 0.1024 | Arginine | 0.0821 |
| | Palmitoleate(C16) | 0.1163 | Laurate(C12) | 0.0959 |
| | glycerol(-H) | 0.1179 | Palmitoleate(C16) | 0.1004 |
| | Oleate(C18) | 0.1202 | Myristate(C14) | 0.1006 |
| adenine | guanine | 0.0626 | guanine | 0.0388 |
| | 7H-purine | 0.0712 | 7H-purine | 0.0701 |
| | cytosine | 0.0840 | benzimidazole | 0.0743 |
| | uracil | 0.0854 | 1H-indazole | 0.0747 |
| | benzopyrimidine | 0.0860 | benzoxazole | 0.0775 |

FIG. 14A

Results for Six Query Compounds, 1-D Shape Signature Self-Comparison of Tripos Fragment Database using $L_1$ Metric

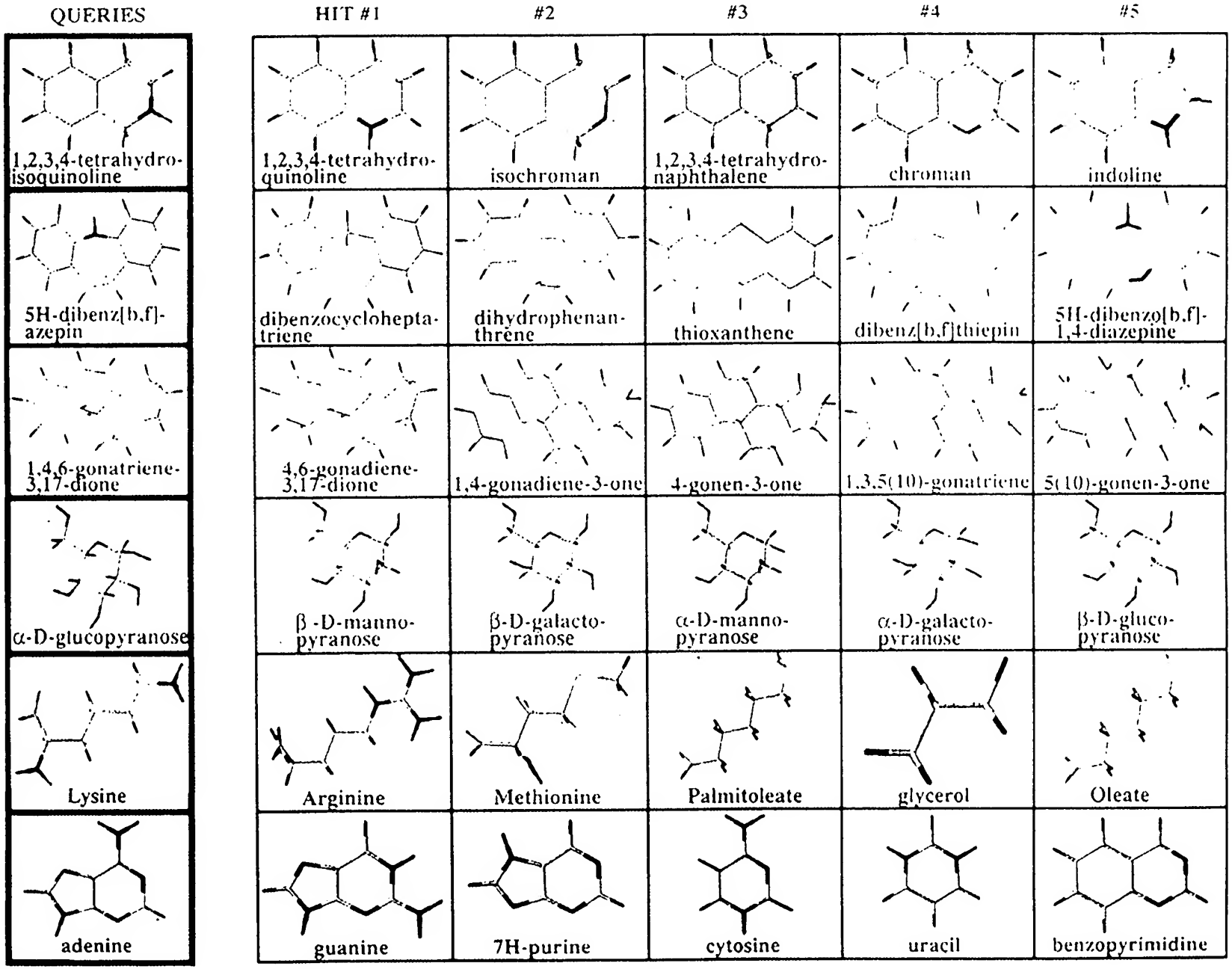



FIG. 14B

. Results for Six Query Compounds, 2D-MEP Shape Signature Self-Comparison of Tripos Fragment Database using $L_1$ Metric

| QUERY | Culling | | No Culling | |
|---|---|---|---|---|
| | Hit | Score | Hit | Score |
| 1,2,3,4-tetrahydroisoquinoline | 1,2,3,4-tetrahydroquinoline | 0.0847 | 1,2,3,4-tetrahydroquinoline | 0.0762 |
| | 1,2,3,4-tetrahydronaphthalene | 0.1496 | 1,2,3,4-tetrahydronaphthalene | 0.1307 |
| | indoline | 0.1732 | indoline | 0.1320 |
| | acenaphthene | 0.1908 | indan | 0.1554 |
| | indan | 0.2161 | acenaphthene | 0.1804 |
| 5H-dibenz[b,f]azepin | dibenzocycloheptatriene | 0.1116 | dibenzocycloheptatriene | 0.1031 |
| | acridan | 0.2089 | acridan | 0.1538 |
| | 5H-dibenzo[b,f]-1,4-diazepine | 0.2109 | 5H-dibenzo[b,f]-1,4-diazepine | 0.1672 |
| | 1,2,3,4-tetrahydroisoquinoline | 0.2268 | phenanthridine | 0.1762 |
| | 1,2,3,4-tetrahydroquinoline | 0.2292 | dihydrophenanthrene | 0.1802 |
| 1,4,6-gonatriene-3,17-dione | 4,6-gonadiene-3,17-dione | 0.0888 | 4,6-gonadiene-3,17-dione | 0.0852 |
| | 5a-gonane-3,17-dione | 0.1383 | 5a-gonane-3,17-dione | 0.1383 |
| | 1,4-gonadien-3-one | 0.2028 | 1,4-gonadien-3-one | 0.2097 |
| | 5a-gonan-3-one | 0.2031 | 4-gonen-3-one | 0.2122 |
| | 5a-gonan-17-one | 0.2211 | 5a-gonan-3-one | 0.2221 |
| 2-deoxy-β-D-ribofuranose | β-D-ribofuranose | 0.2292 | β-D-glucopyranose | 0.2223 |
| | β-D-glucopyranose | 0.2368 | α-D-fructofuranose | 0.2317 |
| | α-D-fructofuranose | 0.2480 | α-D-mannopyranose | 0.2437 |
| | α-D-galactopyranose | 0.2616 | β-D-ribofuranose | 0.2445 |
| | α-D-mannopyranose | 0.2696 | α-D-glucopyranose | 0.2575 |
| Lysine | Arginine | 0.6615 | Arginine | 0.6617 |
| | ethanolamine | 0.7882 | ethanolamine | 0.7621 |
| | choline | 1.2682 | choline | 1.2442 |
| | D-Threose | 1.5332 | D-Threose | 1.4601 |
| | D-Xylose | 1.5667 | D-Xylose | 1.4912 |
| adenine | pteridine | 0.4025 | benzothiazole | 0.3493 |
| | benzothiazole | 0.4321 | pteridine | 0.3816 |
| | guanine | 0.4394 | thiazole | 0.3981 |
| | 7H-purine | 0.4427 | 7H-purine | 0.4254 |
| | indene | 0.4614 | guanine | 0.4265 |

FIG. 15

. Results for Six Query Compounds, 1D Shape Signature Comparison of Tripos Fragment Database against the NCI Database using $L_1$ and $R_1$ Metrics

| QUERY | $L_1$ Metric | | $R_1$ Metric | |
|---|---|---|---|---|
| | Hit | Score | Hit | Score |
| 1,2,3,4-tetrahydroisoquinoline | 91-21-4 | 0.0291 | 91-21-4 | 0.1153 |
| | 10500-57-9 | 0.0336 | 10500-57-9 | 0.1409 |
| | 529-35-1 | 0.0348 | 578-54-1 | 0.1428 |
| | 578-54-1 | 0.0380 | 493-05-0 | 0.1534 |
| | 24206-39-1 | 0.0397 | 529-35-1 | 0.1743 |
| 5H-dibenz[b,f]azepin | 833-48-7 | 0.0324 | 833-48-7 | 0.1404 |
| | 1211-06-9 | 0.0360 | 1211-06-9 | 0.1673 |
| | 10354-00-4 | 0.0415 | 10354-00-4 | 0.1789 |
| | 82-53-1 | 0.0441 | 42263-75-2 | 0.2142 |
| | 6279-16-9 | 0.0488 | 51087-02-6 | 0.2300 |
| 1,4,6-gonatriene-3,17-dione | 24640-00-4 | 0.0450 | 6126-58-5 | 0.2289 |
| | 10448-96-1 | 0.0556 | 24640-00-4 | 0.2561 |
| | 438-67-5 | 0.0570 | 6968-06-5 | 0.2672 |
| | 5976-74-9 | 0.0576 | 20919-82-8 | 0.2908 |
| | 6126-58-5 | 0.0584 | 3601-97-6 | 0.2963 |
| α-D-glucopyranose | 488-66-4 | 0.0546 | 74561-03-8 | 0.2223 |
| | 23559-36-6 | 0.0548 | 488-66-4 | 0.2548 |
| | 74561-03-8 | 0.0553 | 488-64-2 | 0.2548 |
| | 16505-91-2 | 0.0607 | 6623-68-3 | 0.2548 |
| | 39392-65-9 | 0.0655 | 2037-48-1 | 0.2549 |
| Lysine | 5329-79-3 | 0.0478 | 37149-01-2 | 0.1874 |
| | 110-97-4 | 0.0486 | 6963-39-9 | 0.1882 |
| | 5343-35-1 | 0.0552 | 110-97-4 | 0.2107 |
| | 37149-01-2 | 0.0555 | 6281-43-2 | 0.2201 |
| | 7356-00-5 | 0.0563 | 104-50-7 | 0.2224 |
| adenine | 10325-61-8 | 0.0271 | 10325-61-8 | 0.0944 |
| | 54346-27-9 | 0.0304 | 54346-27-9 | 0.0988 |
| | 73-24-5 | 0.0310 | 5426-35-7 | 0.1178 |
| | 1123-54-2 | 0.0343 | 73-24-5 | 0.1178 |
| | 2227-98-7 | 0.0353 | 19165-47-0 | 0.1178 |

FIG. 16A

Results for Six Query Compounds, 1-D Shape Signature Comparison of Tripos Fragment Database vs. NCI

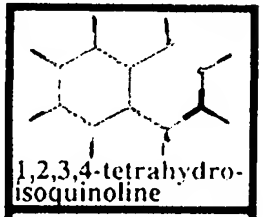
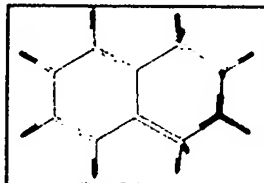
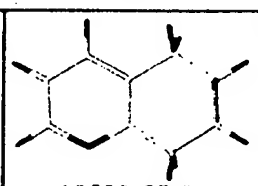
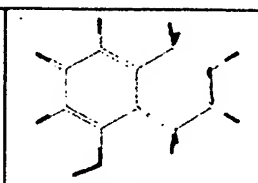
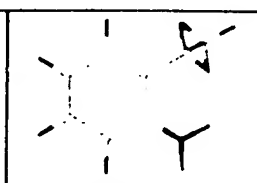
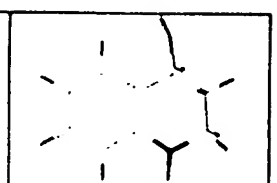
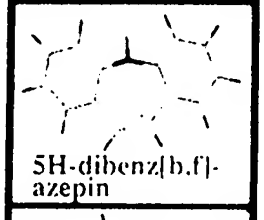
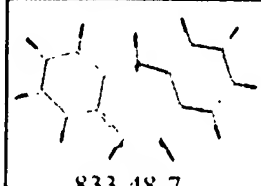
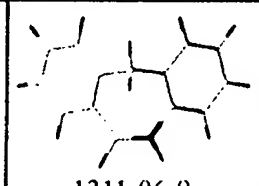
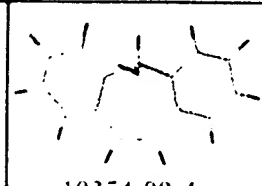
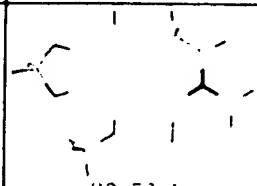
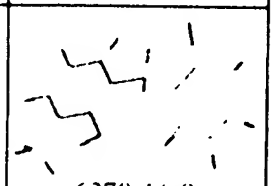
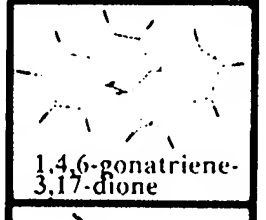
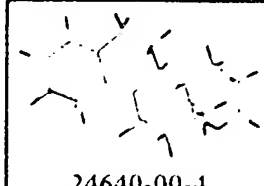
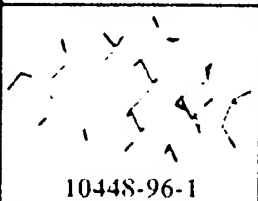
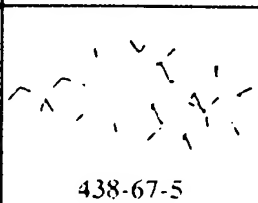
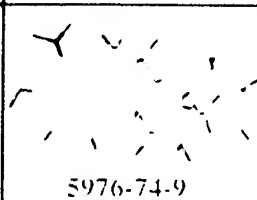
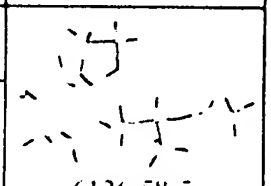
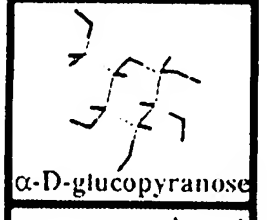
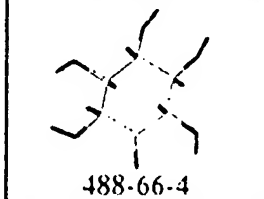
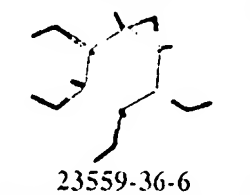
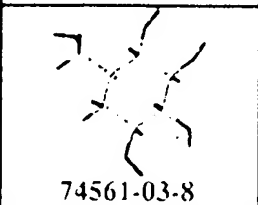
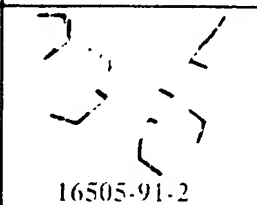
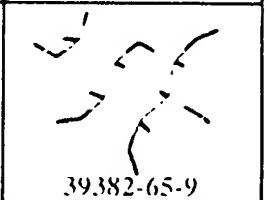
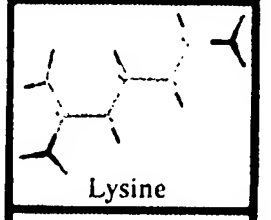
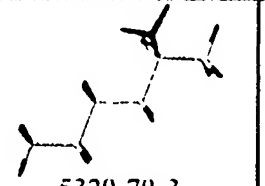
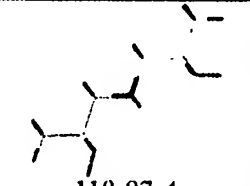
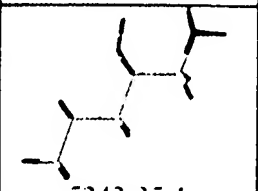
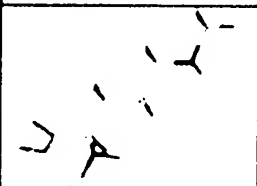
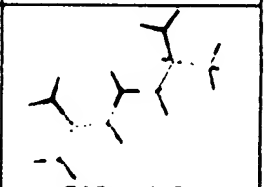
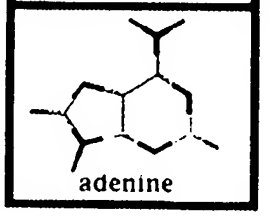
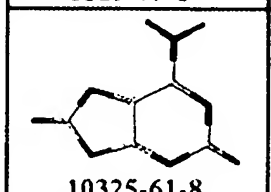
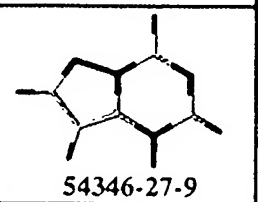
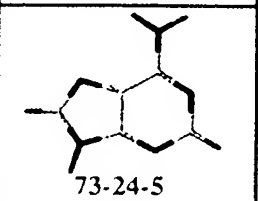
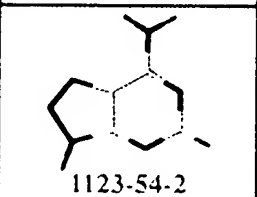
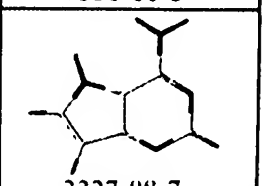
| QUERIES | HIT #1 | #2 | #3 | #4 | #5 |
|---|---|---|---|---|---|
|  1,2,3,4-tetrahydro-isoquinoline |  91-21-4 |  10500-57-9 |  529-35-1 |  578-54-1 |  24206-39-1 |
|  5H-dibenz[b,f]-azepin |  833-48-7 |  1211-06-9 |  10354-00-4 |  82-53-1 |  6279-16-9 |
|  1,4,6-gonatriene-3,17-dione |  24640-00-4 |  10448-96-1 |  438-67-5 |  5976-74-9 |  6126-58-5 |
|  α-D-glucopyranose |  488-66-4 |  23559-36-6 |  74561-03-8 |  16505-91-2 |  39382-65-9 |
|  Lysine |  5329-79-3 |  110-97-4 |  5343-35-1 |  37149-01-2 |  7356-00-5 |
|  adenine |  10325-61-8 |  54346-27-9 |  73-24-5 |  1123-54-2 |  2227-98-7 |

FIG. 16B

. Results for Six Query Compounds, 2D-MEP Shape Signature Comparison of Tripos Fragment Database against the NCI Database using $L_1$ and $R_1$ Metrics

| QUERY | $L_1$ Metric | | $R_1$ Metric | |
|---|---|---|---|---|
| | Hit | Score | Hit | Score |
| 1,2,3,4-tetrahydroisoquinoline | 91-21-4 | 0.0701 | 91-21-4 | 0.5232 |
| | 635-46-1 | 0.0816 | 635-46-1 | 0.6553 |
| | 1484-19-1 | 0.0940 | 1484-19-1 | 0.6977 |
| | 1780-19-4 | 0.0983 | 5344-99-0 | 0.7295 |
| | 5344-99-0 | 0.1011 | 1780-19-4 | 0.8070 |
| 5H-dibenz[b,f]azepin | 30646-39-0 | 0.0947 | 30646-39-0 | 0.8078 |
| | 16886-10-5 | 0.1079 | 3377-71-7 | 0.9075 |
| | 32446-13-2 | 0.1089 | 16886-10-5 | 0.9104 |
| | 3377-71-7 | 0.1126 | 32446-13-2 | 0.9166 |
| | 833-48-7 | 0.1167 | 833-48-7 | 0.9411 |
| 1,4,6-gonatriene-3,17-dione | 56763-86-1 | 0.1524 | 20056-05-7 | 1.3418 |
| | 734-32-7 | 0.1645 | 56763-86-1 | 1.3451 |
| | 93998-31-3 | 0.1682 | 74924-17-7 | 1.4169 |
| | 20056-05-7 | 0.1693 | 734-32-7 | 1.4949 |
| | 74924-17-7 | 0.1702 | 71837-43-9 | 1.5131 |
| α-D-glucopyranose | 52019-14-4 | 0.1815 | 52019-14-4 | 1.4065 |
| | 49871-87-6 | 0.1833 | 58691-27-3 | 1.4270 |
| | 58691-27-3 | 0.1912 | 49871-87-6 | 1.4514 |
| | 7404-25-3 | 0.2015 | 2280-44-6 | 1.5418 |
| | 14215-77-1 | 0.2018 | 14215-77-1 | 1.5520 |
| Lysine | 42021-74-9 | 0.5473 | 85385-47-3 | 4.1381 |
| | 58048-33-2 | 0.5549 | 58048-33-2 | 4.2359 |
| | 58048-35-4 | 0.5684 | 42021-74-9 | 4.2441 |
| | 37082-52-3 | 0.5719 | 78582-26-0 | 4.3301 |
| | 78582-26-0 | 0.5721 | 62194-88-1 | 4.3458 |
| adenine | 73-24-5 | 0.0683 | 73-24-5 | 0.5048 |
| | 28128-33-8 | 0.1537 | 28128-33-8 | 1.0824 |
| | 7390-62-7 | 0.1581 | 7390-62-7 | 1.2106 |
| | 2846-89-1 | 0.1744 | 2846-89-1 | 1.2491 |
| | 3647-48-1 | 0.1820 | 1904-98-9 | 1.2947 |

FIG. 17A

Results for Three Query Compounds, 2D-MEP Shape Signature, Tripos Fragment Database vs. NCI

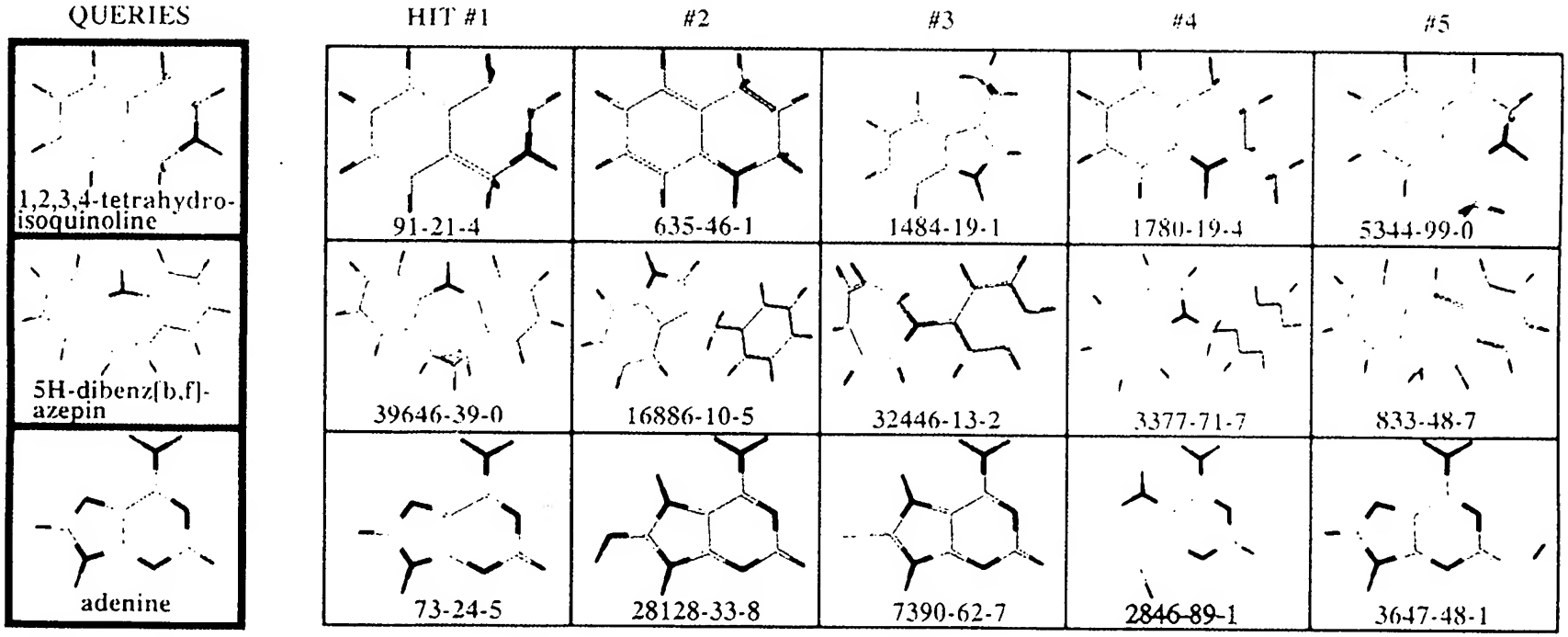



FIG. 17B

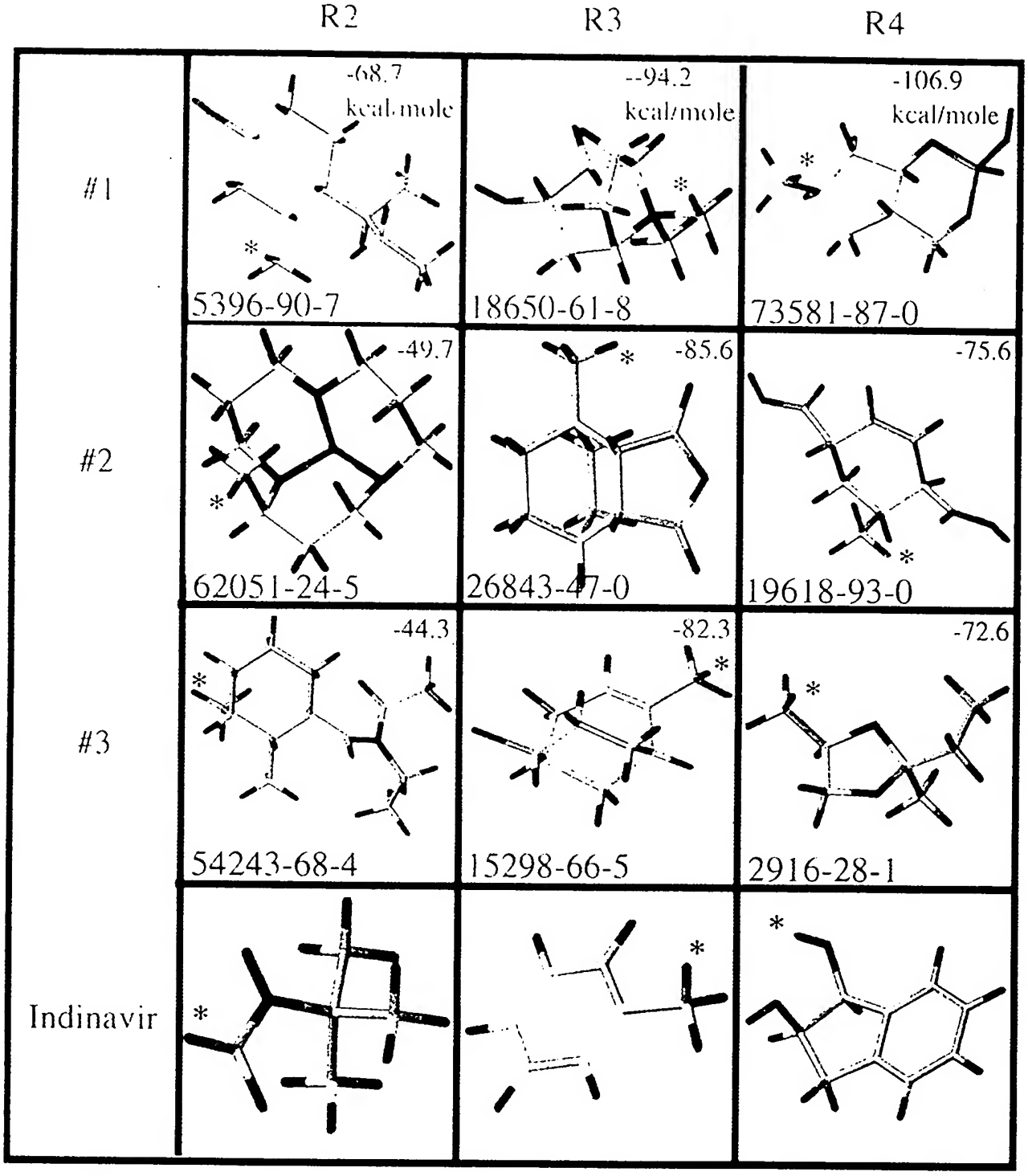

R2
R3
R4
#1
#2
#3
Indinavir
-68.7 kcal/mole
--94.2 kcal/mole
-106.9 kcal/mole
5396-90-7
18650-61-8
73581-87-0
-49.7
-85.6
-75.6
62051-24-5
26843-47-0
19618-93-0
-44.3
-82.3
-72.6
54243-68-4
15298-66-5
2916-28-1

FIG. 18

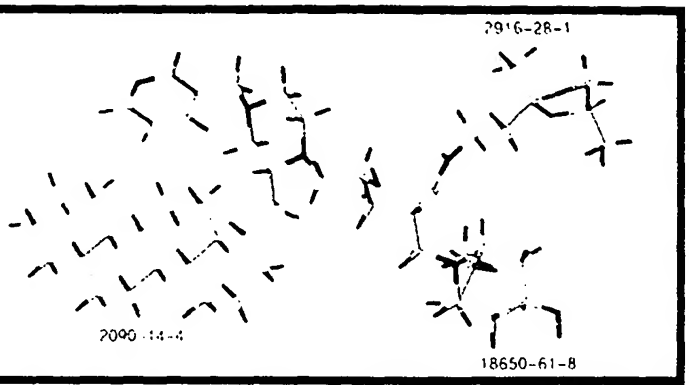
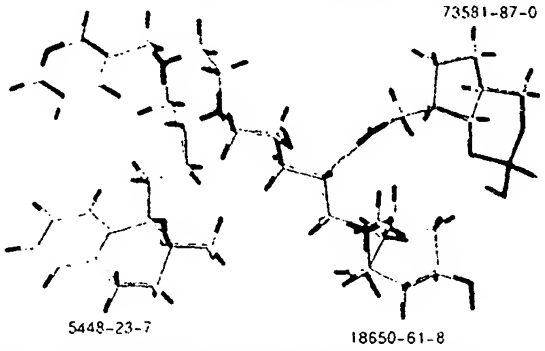
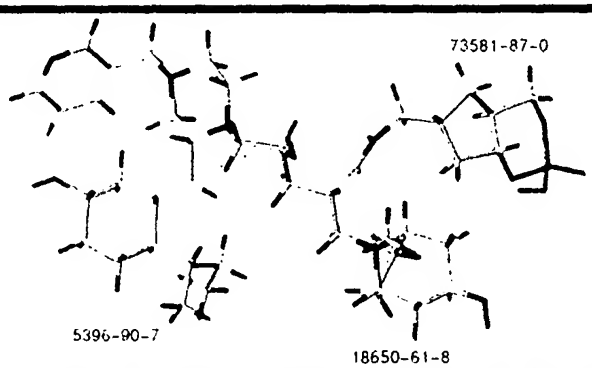
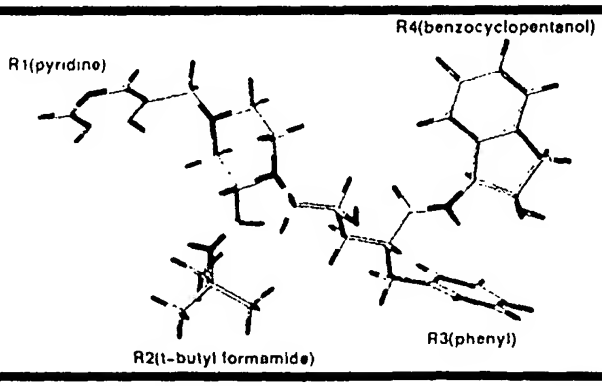
| Rank | Energy(kcal/mol) | Structure |
|---|---|---|
| #1 | -117.3 |   |
| #2 | -117.0 |   |
| #4 | -115.2 |   |
| Indinavir | -97.2 |   |

FIG. 19